

**REMARKS**

Claims 1-3, 5-36, 41-43, and 46 are pending in this application, with claims 8-15, 17-20, 22-36, and 41-43 withdrawn from examination. By this Amendment, claims 1-3, 5-16, 19-24, 30, and 46 are amended and claims 4, 37-40, 44, 45, 47, and 48 are canceled. In addition, the specification is amended to add section titles and a brief description of Figures 1 and 2. Support for the brief description of Figures 1 and 2 is found in, for example, the specification at pages 6 and 13, respectively. The sequence identifiers associated with the amino acid sequences in Figure 2 are set forth in the substitute sequence listing, filed herewith, as SEQ ID NOS: 34-36. Support for SEQ ID NOS: 34-36 is found in, for example, Figure 2 as filed. No new matter is added.

On page 2 of the Office Action, in the section entitled "Election/Restrictions," the Examiner referenced Applicants' reply filed February 2, 2006, and the restriction of February 2, 2005. Applicants assume that the intended dates are February 24, 2006, and February 2, 2006, respectively. If this assumption is incorrect, Applicants request clarification of the intended dates.

On page 3 of the Office Action, in the section entitled "Claim note," the Examiner stated that, prior to allowance, claim 21 must be amended such that it no longer depends from non-elected claims. In response, Applicants amended claim 21 to depend on elected claim 7.

**Sequence Compliance**

The Examiner stated that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 because the sequences in Figure 2 are not identified by sequence identification numbers and are not part of the sequence listing.

In response, a substitute sequence listing is filed herewith adding SEQ ID NOS: 34-36, which correspond to the three amino acid sequences in Figure 2. The nucleotide sequence in Figure 2 is identified in the sequence listing as SEQ ID NO: 1, as described in the

specification at page 13, lines 12-14. As requested by the Examiner, all the sequences in Figure 2 are described in the Brief Description of the Figures.

The attached paper copy and computer-readable copy of the sequence listing are submitted in compliance with 37 C.F.R. §§1.821-1.825. The contents of the paper copy and the computer-readable copy of the sequence listing are the same. No new matter is added.

**Objections**

1. Claim 21 is objected to as "specifically reciting non-elected subject matter," i.e., the phrase "transcription/translation product" (Office Action, p. 4). The Examiner stated that, prior to allowance, claim 21 must be amended such that it no longer contains non-elected subject matter.

In response, Applicants amended claim 21 to recite "transcription product."

2. The disclosure is objected to because it does not contain a section entitled "Brief Description of the Drawings," including a description of Figures 1 and 2 referencing the relevant sequence identification numbers.

In response, Applicants amended the specification as described above.

**Rejection under 35 U.S.C. §101**

Claims 1-7, 16, 21, 37-40, and 44-48 are rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. Applicants respectfully traverse the rejection.

Solely in an effort to further prosecution and without acquiescing in the propriety of the rejection, Applicants amended claims 1-3, 5-7, 16, 21, and 46 to clarify that the claimed products are not products of nature. Applicants appreciate the Examiner's helpful suggestions.

In view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

**Rejection under 35 U.S.C. §112, second paragraph**

Claims 1-7, 16, and 37-40 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Specifically, the rejection is based on an alleged lack of clarity in the phrase "not belonging to SEQ ID NO: 1 and encoding an expression product." Applicants respectfully traverse the rejection.

Solely in an effort to further prosecution and without acquiescing in the propriety of the rejection, Applicants amended claim 1, which contained the allegedly unclear phrase, to clarify that the isolated nucleic acid sequence comprises SEQ ID NO: 2, a sequence encoding an expression product (SEQ ID NO: 31), or a complement thereof. Applicants appreciate the Examiner's helpful suggestion.

In view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

**Rejection under 35 U.S.C. §112, first paragraph**

Claims 1-7, 16, 21, 37-40, and 44-48 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the enablement requirement. Applicants respectfully traverse the rejection.

The rejection is based on Applicants' alleged failure to describe the claimed subject matter in such a way as to enable one skilled in the art to make and/or use the invention. Although the Examiner acknowledged that the rejected claims are product claims, the rejection addresses the functional limitations, e.g., "an association with disease," recited in the claims and asserted in the specification<sup>1</sup> (Office Action, p. 6). According to the Examiner,

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<sup>1</sup> Although the claims are viewed in light of the specification, it must be remembered that it is the claims that are examined, not the specification. It is impermissible to import subject matter from the specification into the claims. *See MPEP §2111.*

the specification fails to describe nucleic acids associated with an autoimmune disease, unsuccessful pregnancy, or pathological conditions of pregnancy. However, no evidence is provided to support the alleged failure and, in the absence of evidence to the contrary, Applicants' statements must be excepted as true. *See* MPEP §2164.04.

On page 7 of the Office Action, the Examiner stated that the specification "teaches that applicant envisages the potential role of retroviral type structures in the development of autoimmune disease, in unsuccessful pregnancy or [in] pathological conditions of pregnancy." This statement, found in the specification on page 2, lines 18-23, refers to the description in Applicants' previous patent application PCT/FR98/01442, incorporated by reference (corresponding to U.S. Patent Application No. 09/446,024, also incorporated by reference), of screening a placenta cDNA library using the Ppol-MSRV probe (SEQ ID NO: 18) and conducting a blastn comparison that showed a considerable number of related genomic sequences.

Also on page 7 of the Office Action, the Examiner used the term "presumably" in regard to SEQ ID NO: 30. Applicants confirm that the sequence of "the reconstructed genome" is set forth in SEQ ID NO: 30.

On page 8 of the Office Action, the Examiner stated that "no genomic fragments identified by database searching contained a 'functional gag gene.'" However, this is not correct. In the specification, page 6, lines 19-20, Applicants state that "[n]o clone contained the *three* functional gag, pol and env open reading frames" (emphasis added).

Also on page 8 of the Office Action, the Examiner indirectly requested clarification of the relationship between SEQ ID NO: 2 and SEQ ID NO: 3. As noted by the Examiner, these sequences are not identical. SEQ ID NO: 2 is a 2009 bp fragment encoding the *gag* gene. The encoded *gag* gene begins at position 434 and ends at position 1522. SEQ ID NO: 3 is the

1056 bp sequence of the probe Pgag-C12, which contains the 1056 bp coding region of the clone MSRV C12. *See* specification, p. 10, Ex. 1; p. 18, last paragraph.

The Examiner asserted that the specification does not disclose the amplification of a *gag* gene from a person not having multiple sclerosis. The relevance of such alleged non-disclosure is not understood. The nucleic acid fragments, upon which the claims depend, have specific sequences associated with autoimmune disease, particularly, multiple sclerosis, unsuccessful pregnancy, or pathological conditions of pregnancy. The sequence of a non-MS genome is simply unnecessary to make and use the claimed invention.

The Examiner further asserted that the specification does not provide results of various analyses (Office Action, p. 9). Again, the relevance of such alleged non-disclosure is not understood. Moreover, regarding the amplification product analysis, Applicants state that the PCR products were analyzed, transferred to a nylon membrane for hybridization, cloned in pCR® 2.1-TOPO vector, and sequenced using the PRISM™ Ready Reaction AmpliTaq® FS, DyeDeoxy™ Terminator sequencing kit (specification, p. 17, line 33-p. 18, line 32). A similar description of PCR products and their amplification is set forth on page 1871, column 1, in Mayer, J. et al., *Journal of Virology* 72(3): 1870-75 (March 1998) ("Mayer"), cited by the Examiner. It is not clear what additional analysis would be needed by one skilled in the art, especially since the highly skilled artisan<sup>2</sup> would be intimately familiar with PCR technology. Thus, Applicants need not provide additional details of this technique in the patent application. It is the specification *combined with* the knowledge in the art that needs to, and does in this case, provide sufficient information such that one skilled in the art can practice the claimed invention without undue experimentation.

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<sup>2</sup> As noted by the Examiner, "the state of the art with regard to identification or production of any nucleic acid of a particular sequence is high" (Office Action, p. 10).

Regarding the transcription/translation analysis, again, the relevance of such analysis, or lack thereof, is not understood. As noted by the Examiner, the protein products are described in Table 2 by molecular mass and human chromosome number. A method of obtaining the protein products is set forth in Example 2.2. The particular method described is the In Vitro Transcription/Translation Test ("PTT" by Promega) - another well-known test in this highly skilled art. *See, e.g.*, Mayer, p. 1871, col. 1. Thus, it is not clear what additional analysis would be needed by one skilled in the art. It is also not clear why the Examiner finds it "notable" that the PCR products were used as templates in the in vitro PTT and sequenced, but the results of the sequencing analysis and the source of the "mass heterogeneity" are not disclosed (Office Action, p. 9).

The Examiner stated that the specification does not define the source of the neurological control samples nor provide statistical interpretation of the data such that the significance of the results can be determined. The Examiner subsequently stated that the specification does not provide an analysis of nucleic acids or transcripts from a diseased sample compared to a non-diseased control sample. In response, Applicants refer to the specification, Example 3, pages 22-23. The neurological controls are known, and the non-diseased control samples are known (abbreviated "BTC," which stands for blood transfusion center control sera).

Regarding "statistical interpretation," the use of "+" and "-" signs is common and readily understood, and, regardless, Applicants do provide an interpretation, i.e., approximately 40%, in the last paragraph on page 23. It must be remembered that a patent application is not an FDA application to conduct clinical trials.

Regarding sequence analysis, the Examiner stated that there is no analysis of fragments of SEQ ID NO: 2 and "no indication of the different expression of any transcription or translation product belonging to SEQ ID NO: 2 but not SEQ ID NO: 1" (Office Action, p.

10). In response, Applicants assert that such analysis is described in the specification, specifically Example 3, which employs a fragment of SEQ ID NO: 2, i.e., the coding region of the *gag* gene. Second, it is not clear why the specification needs to contain an analysis of sequences from nucleic acid fragments that are *not claimed*.

The Examiner next stated that the association between the nucleic acid fragments and a disease is not shown in a "statistically significant manner." More specifically, the Examiner asserted that neither the specification nor the prior art indicates that the SEQ ID NO: 2 fragment containing bp 374-473 is associated with a disease or pathological condition (Office Action, p. 11).

In response, Applicants contend that claim 1 is *not* limited to the single fragment from SEQ ID NO: 2 spanning bp 374-473. Second, the prior art does not indicate the asserted association because the determination of the association between the nucleic acid fragments set forth in the claims and the described diseases and conditions is not taught in the prior art. Third, the specification does explain the asserted association in, for example, the Examples. Fourth, Applicants are not required to produce "statistically significant" results. As noted above, a patent application is not an FDA submission.

According to the Examiner, one skilled in the art cannot predict whether the claimed nucleic acid fragments, which encompass fragments associated with diseases or conditions in any organism, would be applicable to species other than human. The Examiner cited Mayer, *supra*, to support this position.

First, Applicants request clarification of the Examiner's comments. Is the Examiner asserting that the claims need to be limited to humans? If so, this aspect of the rejection is not understood because, among other reasons, the rejected claims are product claims, i.e., nucleic acid molecules or products based on these molecules, derived from *human* DNA as indicated in the sequence listing.

Second, Applicants respectfully disagree that Mayer supports the Examiner's position, which Applicants presume is that the claimed nucleic acid molecules cannot be obtained from non-human species. Mayer is directed to the ability of a specific retrovirus to survive evolution. In Mayer's Figure 6, referenced by the Examiner on page 11 of the Office Action, Mayer compares the HERV-K *gag* gene's central region from two lower Old World primate species - African green monkey and crab-eating macaque - to the HERV-K10 *gag* region isolated from a human. Mayer states that the three primate species' sequences were "highly homologous" (p. 1873, col. 1); and the only notable distinction between the Old World primates' sequences and the human sequence was the 96 bp deletion in the human DNA. Mayer explains that lower Old World primates, i.e., African green monkey, crab-eating macaque, gelada, hamadryas, and rhesus monkey, have a larger HERV-K *gag* gene than that found in hominid species, i.e., human, chimpanzee, gorilla, and orangutan, due to a deletion that "most likely resulted from a mutational event during Old World primate evolution" (p. 1873, col. 2). This "mutational event occurred immediately after the *Hominidae* tribe separated from the lower Old World primates" (p. 1873, col. 2). Further, Mayer states that, "[a]s shown in this study, full-length HERV-K *gag* genes are present in all Old World primates" and "[a]ll species except *P. troglodytes* [chimpanzee], possess ORFs for Gag protein" (p. 1874, col. 1). The partial deletion of the *gag* sequence in the hominid species, i.e., the "missing" 96 bp within the *gag* gene, may have caused a modification, but does *not affect the ORF* (p. 1874, col. 1).

To support the position that the specification does not enable the association of the claimed nucleic acid fragments with a disease or disorder, the Examiner cited Newton, M.A. et al., *Journal of Computational Biology* 8(1): 37-52 (2001) ("Newton"). According to the Examiner, Newton teaches "the difficulty in applying gene expression results to the association of gene expression with a phenotype" (Office Action, p. 11).

The Examiner's position is not understood by Applicants. The Newton article, entitled "On Differential Variability of Expression Ratios: Improving Statistical Inference about Gene Expression Changes from Microarray Data," describes the use of cDNA microarrays to monitor gene expression on a genome-wide scale. What is measured is the *amount* of cDNA in a synthetic population of nucleic acid molecules that corresponds to the mRNA composition of a particular cell. There is no indication in Newton that sera reactivity to recombinant proteins is not indicative of nucleic acid expression. Moreover, in Example 3 in the specification, Applicants demonstrate reactivity, and thus expression, using the well-known technique of Western Blotting, whereby proteins are detected by, for example, labeled antibodies. As discussed on page 23 of the specification, Applicants employed alkaline phosphatase-coupled anti-human IgG and IgM goat serum and detected reactivity in the sera from patients having multiple sclerosis.

The Examiner also cited Chan, E., *Genomics & Proteomics* (internet publication dated April 1, 2006) ("Chan") to support the position that it is unpredictable whether the claimed nucleic acid fragments and transcription products are "associated with any disease or pathological condition" (Office Action, p. 12).

The Examiner's reliance on Chan is not understood. The Chan publication is an advertisement for Rosetta Biosoftware's microarray software used to integrate transcriptome and proteome profiles and the lack of concordance between the two when analyzed separately. That lack of concordance is in terms of quantification, not protein identification. Chan, a data analyst for Rosetta Biosoftware, presents theories about the discord between transcript *expression* and protein level as exemplified by the statement at the top of page 4, "[t]he challenge here is not to draw a one-to-one correlation between mRNA and protein *levels*; rather, the challenge is to distinguish true positives, be it true mRNA-protein concordance or discordance, from false positives" (emphasis added). One example that

follows this statement is the mammalian 24-hour circadian clock regulated by, *inter alia*, the protein Period, which has a 4 to 8 hour delay between protein and transcript expression. In other words, the amount of relevant mRNA does not correspond to the Period protein level when compared at certain times. Thus, Chan fails to support the Examiner's position.

The third article cited in support of the rejection is Lucentini, J., *The Scientist* 18(24): 20 (Dec. 20, 2004) ("Lucentini"), which claims that gene-disease associations are "few and far between." The article focuses on gene-disease association studies, which do not equate to patent applications linking protein expression with a particular type of disease or condition. In addition, Lucentini discusses meta-analyses, which do not equate to the analysis set forth in Examples 1-3 in the specification. Thus, Lucentini does not support the premise for which it was cited.

The final article relied on by the Examiner is by Ronald A. Thisted, Ph.D. ("What is a P-value?", pp. 1-6 (May 25, 1998) ("Thisted")), a professor of statistics. Again, the Examiner's reliance is not understood. Thisted analyzes the statistical P-value and its use in *clinical trials* comparing placebo treatments with active drug treatments. A patent application is not an FDA application. Examples 1-3 in the specification are not clinical trials. Thus, Thisted also does not support the premise for which it was cited.

The Examiner's final argument centers on an alleged "large and prohibitive amount of experimentation" necessary to make and use the claimed invention (Office Action, p. 13). Applicants do not understand why one skilled in the art would need to analyze "many possible different organisms, and also ... a large number of diseases" in a "large case:control study" (Office Action, p. 13). The claimed products are, or are derived from, nucleic acid molecules having a particular sequence as set forth in claim 1. It is not clear what type of "large case:control study" the Examiner envisions.

As discussed at length above, the focus of the rejection is on the functional limitations of the nucleic acid fragments. However, the functional limitations carry little, if any, weight in the rejections under 35 U.S.C. §102. *See* Office Action, p. 14. It is respectfully submitted that the Examiner cannot have it both ways. In other words, functional limitations of a product cannot carry significant weight in an enablement rejection, yet, at the same time, carry little, if any, weight in an anticipation rejection. Claim interpretation should not, and does not, depend on the particular statute at issue. Instead, under both statutes, functional limitations only come into play when deletion thereof from a claim affects the structure or steps recited in the claim. *See* MPEP §2111.02(II).

In the claims at issue, the allegedly non-enabled functional limitations, i.e., "autoimmune disease," "unsuccessful pregnancy," and "pathological conditions of pregnancy," are not claim-limiting, as implied by the Examiner, because the nucleic acid fragments, reagents, and transcription products claimed would be unaffected by the absence of such "limitations." In other words, claim 1, for example, would remain directed to an isolated nucleic acid molecule having a particular sequence. Therefore, although unnecessary, in an effort to expedite prosecution, and without acquiescing in the propriety of the rejection, claims 37-40, 44, 47, and 48 are canceled and claims 1, 16, and 21 are amended such that the allegedly non-enabled functional limitations, i.e., "autoimmune disease," "unsuccessful pregnancy," and "pathological conditions of pregnancy," are no longer explicitly recited.

Claim 1 is directed to an isolated nucleic acid molecule having a sequence of an endogenous retrovirus *gag* gene. That sequence comprises: SEQ ID NO: 2 (or a sequence complementary thereto); or a sequence that encodes an expression product, the sequence of which comprises SEQ ID NO: 31 (or a sequence complementary thereto).

SEQ ID NO: 2 is the sequence of the 2009 bp fragment encoding the *gag* gene. The encoded *gag* gene begins at SEQ ID NO: 2, position 434 and ends at SEQ ID NO: 2, position 1522, and is set forth in SEQ ID NO: 31, as stated in the specification, page 18, lines 34-36 (as previously amended). Example 2.1, pages 16-19, describes in great detail how to obtain the 2009 bp fragment of SEQ ID NO: 2.

In view of the fact that SEQ ID NO: 2 and SEQ ID NO: 31 are described in detail in the specification, Applicants respectfully assert that the specification provides more than sufficient guidance for one skilled in the art to make the nucleic acid molecules of claim 1, the transcription products of claim 7, and the reagents of claim 21 without undue experimentation.

Additionally, in view of the fact that the specification describes numerous uses of the nucleic acid molecules, Applicants respectfully assert that the specification provides more than sufficient guidance for one skilled in the art to use the claimed products without undue experimentation. *See, e.g.*, specification, pp. 10-13, 22, and 23.

Because the specification provides sufficient guidance such that one skilled in the art can make and use the claimed invention without undue experimentation, Applicants have satisfied the statutory requirements. It is impermissible for the Examiner to require more than is required by statute. Thus, reconsideration and withdrawal of the rejection are respectfully requested.

**Rejections under 35 U.S.C. §102**

1. Claims 1-6, 16, 37, 38, and 44-48 are rejected under 35 U.S.C. §102(b) as being anticipated by Brennan (U.S. Patent No. 5,474,796) ("Brennan"). Applicants respectfully traverse the rejection.

To anticipate a claim, the applied reference must teach each and every element in the claim. Brennan fails to satisfy this requirement. The Examiner stated that Brennan discloses

an oligonucleotide having the sequence ggaaacattc, which is identical to nucleotides 377-386 of SEQ ID NO: 2.

In response, Applicants first note that the sequence ggaaacattc is not identical to the sequence set forth at nucleotides 377-386 of SEQ ID NO: 2, i.e., ctgggagcaa. Second, the sequence ggaaacattc is not taught by Brennan. Brennan states that the array is synthesized in a 5' to 3' direction, wherein each 5'-most nucleotide is deleted and a new 3'-most nucleotide is added such that "every possible *permutation* of the 10-mer oligonucleotide" is on the array (emphasis added). Brennan, col. 9, lines 49-55. Assuming that Brennan's SEQ ID NO: 1, i.e., attcttgtta, is the Example 3 10-mer, the resulting array contains: attcttgtta, ttcttgttaa, tcttgttaat, ctgttaatt, ttgttaattc, tgttaattct, gttaattctt, ttaattcttg, taattcttgt, aattcttgtt, and attcttgtta, *but not* ggaaacattc.

The Examiner stated that the term "gag protein" is interpreted to mean any part of SEQ ID NO: 31. Office Action, pp. 15-16. Thus, "due to its comprehensive nature," the array disclosed by Brennan inherently discloses part of the gag gene encoding a gag protein. Office Action, p. 16.

Applicants request further clarification of the Examiner's interpretation of Brennan if this rejection is maintained. Brennan does not disclose every single nucleotide combination of any nucleotide sequence, as suggested by the Examiner. Brennan is limited to a description of generating a nucleotide array that contains permutations of a given sequence. One 10-mer is provided as an example. As asserted above, neither that one 10-mer nor its permutations anticipates the claims.

In view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

2. Claims 7, 16, 21, 39, 40, and 44-48 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mayer et al., *Journal of Virology* 72(3): 1870-75 (March 1998) ("Mayer"). Applicants respectfully traverse the rejection.

The Examiner stated that Mayer discloses a nucleic acid fragment consisting of a portion of an endogenous retroviral *gag* gene. The Examiner concluded that the claim phrase "associated with an autoimmune disease, or with unsuccessful pregnancy [or] pathological conditions of pregnancy" is not defined, and thus the nucleic acid fragment disclosed by Mayer anticipates the claims. Office Action, p. 16.

First, Applicants request clarification regarding the rejected claims. Dependent claims 7 (prior to this Amendment), 16, 21, 39, and 40 (and also amended dependent claim 46) are allegedly anticipated by Mayer, but *not* independent claim 1. It is not clear how a reference can anticipate a dependent claim, but not the corresponding independent claim.

Without acquiescing in the propriety of the rejection, Applicants canceled claims 39, 40, 44, and 48 and amended claims 7, 16, and 21 such that the allegedly undefined phrase is no longer present in the claims. Moreover, with regard to independent claim 1, Applicants amended the claim such that the nucleic acid molecule comprises a sequence selected from the group consisting of: (i) SEQ ID NO: 2; (ii) a sequence encoding an expression product, the sequence of which comprises SEQ ID NO: 31; and (iii) a sequence complementary to (i) or (ii). Mayer fails to disclose any member of this Markush group.

In view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

3. Claims 1-7, 16, 21, 37-40, and 44-48 are rejected under 35 U.S.C. § 102(b) as being anticipated by Perron et al. (WO 98/23755) ("Perron"). Applicants respectfully traverse the rejection.

The Examiner stated that SEQ ID NO: 139 disclosed by Perron anticipates the claims, either explicitly or inherently, but the Examiner failed to adequately explain the basis for anticipation. For example, the sequence of SEQ ID NO: 139 is a probe sequence - tgccgctgtgcctgatc. This sequence does not encode any protein or portion thereof. Thus, in order to fit the parameters of the claims, the Examiner changed the sequence to gtccgctctgcctgat and concluded that this "second reading frame" of SEQ ID NO: 139 encodes the polypeptide VRCPD, a combination of six amino acids. Thus, the Examiner based the rejection on the manipulation of a disclosed, non-coding probe sequence into an undisclosed, 6 amino acid coding sequence to conclude that Perron anticipates the claims. Applicants respectfully disagree.

First, it is impermissible for the Examiner to create disclosure in an applied reference to fit the subject matter of a rejected claim.

Second, Perron's SEQ ID NO: 139 does not encode a polypeptide. As noted above, it is a probe sequence.

Third, not only does Perron fail to anticipate the originally filed claims, Perron fails to anticipate the subject matter of the amended claims. Independent claim 1 requires a nucleic acid molecule comprising a sequence selected from the group consisting of: (i) SEQ ID NO: 2; (ii) a sequence encoding an expression product, the sequence of which comprises SEQ ID NO: 31; and (iii) a sequence complementary to (i) or (ii). Perron fails to disclose any member of this Markush group. Because Perron does not anticipate independent claim 1, Perron does not anticipate claims 2, 3, 5-7, 16, 21, and 46.

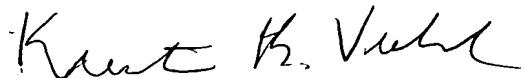
In view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

**Conclusion**

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of, at least, claims 1-3, 5-7, 16, 21, and 46 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



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WPB:KKV/hs

Attachment:

Substitute Sequence Listing (paper copy and computer-readable copy (CRF))

Date: October 23, 2006

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